

Grading TESI: Crypt and villus formation in tissue-engineered small intestine alters with stem/progenitor cell source.

Journal: Am J Physiol Gastrointest Liver Physiol

Publication Year: 2020

Authors: Elizabeth A Gilliam, Christopher R Schlieve, Kathryn L Fowler, Jessica N Rea, Kathy A Schall, Sha Huang, Jason R Spence, Tracy C Grikscheit

PubMed link: 32597710

Funding Grants: Mechanism of Tissue Engineered Small Intestine Formation , The generation and expansion of tissue-engineered small intestine from human stem/ progenitor cells: a preclinical study of functional translation

Public Summary:

The small intestine has a remarkable ability to enhance its absorptive and digestive surface area through the formation of villi, a process known as villification. We sought to learn whether developing mouse and human tissue-engineered small intestine (TESI) followed known developmental biology routes to villification, such as Sonic hedgehog (SHH)/Indian hedgehog (IHH) and bone morphogenetic protein 4 (BMP4)/forkhead box F1 (FOXF1) signaling to identify targets to enhance the development of TESI. After generating TESI from prenatal and postnatal stem cell sources, we evaluated the effect of cell source derivation on villification with a grading scheme to approximate developmental stage. χ^2 analysis compared the prevalence of TESI grade from each stem cell source. RNAscope probes detected genes known to direct villification and the development of the crypt-villus axis in mouse and human development. These were compared in TESI derived from various pluripotent and progenitor cell donor cell types as well as native human fetal and postnatal tissues. Prenatal and pluripotent cell sources form mature villus and crypt-like structures more frequently than postnatal donor sources, and there are alternate routes to villus formation. Human TESI recapitulates epithelial to mesenchymal crosstalk of several genes identified in development, with fetal and pluripotent donor-derived TESI arriving at villus formation following described developmental patterns. However, postnatal TESI is much less likely to form complete villus-crypt patterns and demonstrates alternate SHH/IHH and BMP4/FOXF1 signaling patterns. Grading TESI and other cellular constructs may assist discoveries to support future human therapies. **NEW & NOTEWORTHY** The small intestine can enhance its absorptive and digestive surface area through a process known as villification. Tissue-engineered small intestine achieves mature villification at varying levels of success between differing sources. We have developed a consistent grading schema of morphology and characterized it across multiple developmental pathways, allowing objective comparison between differing constructs and sources.

Scientific Abstract:

The small intestine has a remarkable ability to enhance its absorptive and digestive surface area through the formation of villi, a process known as villification. We sought to learn whether developing mouse and human tissue-engineered small intestine (TESI) followed known developmental biology routes to villification, such as Sonic hedgehog (SHH)/Indian hedgehog (IHH) and bone morphogenetic protein 4 (BMP4)/forkhead box F1 (FOXF1) signaling to identify targets to enhance the development of TESI. After generating TESI from prenatal and postnatal stem cell sources, we evaluated the effect of cell source derivation on villification with a grading scheme to approximate developmental stage. χ^2 analysis compared the prevalence of TESI grade from each stem cell source. RNAscope probes detected genes known to direct villification and the development of the crypt-villus axis in mouse and human development. These were compared in TESI derived from various pluripotent and progenitor cell donor cell types as well as native human fetal and postnatal tissues. Prenatal and pluripotent cell sources form mature villus and crypt-like structures more frequently than postnatal donor sources, and there are alternate routes to villus formation. Human TESI recapitulates epithelial to mesenchymal crosstalk of several genes identified in development, with fetal and pluripotent donor-derived TESI arriving at villus formation following described developmental patterns. However, postnatal TESI is much less likely to form complete villus-crypt patterns and demonstrates alternate SHH/IHH and BMP4/FOXF1 signaling patterns. Grading TESI and other cellular constructs may assist discoveries to support future human therapies. **NEW & NOTEWORTHY** The small intestine can enhance its absorptive and digestive surface area through a process known as villification. Tissue-engineered small intestine achieves mature villification at varying levels of success between differing sources. We have developed a consistent grading schema of morphology and characterized it across multiple developmental pathways,

allowing objective comparison between differing constructs and sources.

Source URL: <https://www.cirm.ca.gov/about-cirm/publications/grading-tesi-crypt-and-villus-formation-tissue-engineered-small-intestine>